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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|------------------------|------------------|
| 10/784,352 | 02/23/2004 | Aaron T. Timperman | 22085/2102 | 2338 |
| 29932 | 7590 | 01/11/2005 | EXAMINER | |
| PALMER & DODGE, LLP PAULA CAMPBELL EVANS 111 HUNTINGTON AVENUE BOSTON, MA 02199 | | | BARTON, JEFFREY THOMAS | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1753 | |

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/784,352

Applicant(s)

TIMPERMAN, AARON T.

Examiner

Jeffrey T. Barton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-12,14,18-24,28-33,37-41 and 43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-12,14,18-24,28-33,37-41 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 November 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of 9 November 2004 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of

5 August 2004

2. All objections to the drawings and specification are withdrawn due to applicant's amendment.
3. All rejections of claims 2-4, 13, 15-17, 25-27, 34-36, and 42 are obviated due to cancellation of the claims.
4. The rejection of claims 1, 6-9, 11, 12, 19-22, 24, 29, 30, 32, 33, 38, 39, and 41 under both 35 U.S.C. §102(e) and 35 U.S.C. §103(a) as anticipated by/obvious over Xue et al is withdrawn due to applicant's amendment.
5. The rejection of claims 5, 18, 28, and 37 under 35 U.S.C. §103(a) as obvious over Xue et al in view of Karger et al is withdrawn due to applicant's amendment.
6. The rejection of claims 10, 23, 31, and 40 under 35 U.S.C. §103(a) as obvious over Xue et al in view of Kopf-Sill et al is withdrawn due to applicant's amendment.
7. The rejection of claims 14 and 43 under 35 U.S.C. §103(a) as obvious over Xue et al in view of Lee et al is withdrawn due to applicant's amendment.

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8. However, rejections on the same grounds presented in the prior action are given below. Due to the incorporation of the limitations of original claims 3, 4, and 13 into claim 1, claims 1, 5-9, 11, 12, 14, 18-22, 24, 28-30, 32, 33, 37-39, 41, and 43 are rejected under 35 U.S.C. §103(a) as obvious over Xue et al in view of Karger et al and Lee et al. Claims 10, 23, 31, and 40 are rejected under 35 U.S.C. 103(a) as obvious over these references and further in view of Kopf-Sill et al.

Claim Objections

9. Claim 5 is objected to because it depends from a cancelled claim (3). The claim is treated herein as though it depended from claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. The rejections presented below are modified from those presented in the prior action, due to the incorporation of limitations from original claims 3, 4, and 13 into independent claim 1. No new grounds for rejection are presented.

12. Claims 1, 5-9, 11, 12, 14, 18-22, 24, 28-30, 32, 33, 37-39, 41, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xue et al in view of Karger et al and Lee et al.

Relevant to claims 1 and 12, Xue et al disclose a microfluidic bi-directional capillary electrophoresis device (Figure 7b), comprising: a middle column (24 and 25), the middle column intersecting a first channel and a second channel (26 and 27) at a point wherein the middle column is approximately perpendicular to the first and second channels (23), a negative electrode in communication with the first channel and a positive electrode in communication with the second channel (33), wherein a mixture of anions and cations may be separated by drawing them towards the electrodes of opposite polarity.

Relevant to claims 24 and 33, Xue et al disclose a method of separating a sample of anions and cations in a microfluidic capillary system, comprising: delivering the sample to the middle column of the device described above in addressing claims 1 and 12 (Paragraph 0071 - sample in 28 and vacuum applied to 29 would lead to sample traveling through channels 24 and 25), positioning negative and positive electrodes (33) in communication with the first and second channels, thereby drawing anions and cations into the channel corresponding to the electrode of opposite polarity (Paragraph 0071, Figure 9)

Relevant to claims 6, 7, 19, 20, 29, 30, 38 and 39, Xue et al disclose first and second detectors in communication with the first and second channels, for the detection of cations and anions, respectively. (Detectors 52 and 53, Figure 7B; Paragraph 0054)

Relevant to claims 8, 21, 32, and 41, Xue et al disclose hydrodynamic flow resistance through variation of cross-sectional area in any or all channels. (Paragraph 0038)

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Relevant to claims 9 and 22, Xue et al disclose devices comprising a pressure outlet. (Paragraphs 0034 and 0040; Line 47, Figure 2)

Relevant to claim 11, Xue et al disclose the first channel being a capillary. (Paragraphs 0038 and 0039; dimensions are such that the channels can be termed capillaries)

Xue et al do not explicitly disclose a coated first channel, a coated second channel, or a first channel engaged to a microfluidic system for proteome analysis (Claims 1, 12, 24, and 33); a first channel coated with Triton X-100 (Claims 5, 18, 28, and 37); or a second channel engaged to a second microfluidic system for proteome analysis. (Claims 14 and 43)

Relevant to claims 1, 12, 24, and 33, Karger et al disclose capillary channels that have been coated with Triton X-100 in order to reduce electroosmosis in electrophoretic separations. (Column 5, lines 3-39)

Relevant to claims 1, 12, 24, and 33, Lee et al disclose microfluidic systems for two-dimensional protein separations in proteome analysis (e.g. Figure 3, Paragraph 0033)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices and methods of Xue et al by coating the first and second channels (26 and 27) with Triton X-100, as taught by Karger et al, because it would reduce electroosmosis. Such coatings would be an obvious modification of the devices and methods of Xue et al, because it would be desirable to minimize electroosmosis in such a system, wherein oppositely charged analytes migrate in

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opposite directions within a channel. Excessive electroosmosis would lead to a bulk flow that prevents migration in one of the directions, or leads to undesirably long migration times, as would be obvious to one having ordinary skill in the art.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the devices and methods of Xue et al by placing the channels (26 and 27) in communication with sample inlets to proteome analysis systems, such as those taught by Lee et al, because it would provide a more powerful analytical tool with an additional dimension of separation. Because Xue et al and Lee et al are directed towards quite similar problems (i.e. separation of proteins by electrophoresis within capillary channels formed on a substrate), the examiner considers that it would have been within the abilities of a skilled artisan to incorporate such known related prior art channel geometries, connectivity, and separation strategies as taught by Lee et al into the system of Xue et al, given a protein sample of sufficient complexity that it would require multiple stages of separation.

13. Claims 10, 23, 31, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xue et al, Karger et al, and Lee et al as applied to claims 1, 12, 24, and 33 above, and further in view of Kopf-Sill et al.

Xue et al, Karger et al, and Lee et al disclose combined devices and methods as disclosed above in addressing claims 1, 12, 24, and 33.

None among Xue et al, Karger et al, and Lee et al explicitly disclose the use of a dual-channel detector in communication with the first and second channels.

Kopf-Sill et al disclose the use of multichannel detectors in communication with one or more channels within their microfluidic device. (Figure 13; Paragraphs 0036 and 0088)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combinations of the devices and methods of Xue et al, Karger et al, and Lee et al by adjusting the position of separation channels such that they ran parallel and adjacent to each other and positioning a dual channel detector in communication with the channels, as taught by Kopf-Sill et al, because it would eliminate the need for multiple detectors.

Response to Arguments

14. Applicant's arguments filed 9 November 2004 have been fully considered but they are not persuasive.

Regarding the limitation to a coating being present within the channels of the device, applicant's arguments are directed towards the Xue et al reference (Amendment Page 12, 3rd full paragraph), although there was no argument in the prior action that a coating was inherently present in the device and methods of Xue et al (Inherency of low charge on channel surfaces was argued). Claims involving coated channels were rejected in view of Karger et al, who teach the usefulness of coating capillary columns in reducing electroosmosis. (Abstract) As stated in the rejection above, such coatings would be an obvious modification of the devices and methods of Xue et al, because it would be desirable to minimize electroosmosis in such a system, wherein oppositely

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charged analytes migrate in opposite directions within a channel. Excessive electroosmosis would lead to a bulk flow that prevents migration in one of the directions, or leads to undesirably long migration times, as would be obvious to one having ordinary skill in the art. Applicant is silent regarding the combination of Xue et al with Karger et al.

Applicant also argues that the disclosure in the specification that the coating reduces sample loss and allows the use of smaller sample sizes further distinguishes the claim from Xue et al, because Xue et al do not address these problems.

(Amendment, Paragraph bridging pages 12-13) Since there is no explicit recitation in the claim regarding these matters, this does not patentably distinguish the claim above the prior art. For example, the Federal Circuit has found that limitations appearing in the specification but not recited in the claim are not read into the claim. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003)

Regarding the limitation that the first coated column engages a microfluidic system for proteome analysis, Applicant presents a lengthy excerpt from the specification to show how the described proteome analysis system is distinct from that of Lee et al. (Amendment pages 13-15) As cited above, the Federal Circuit has ruled that limitations from the specification are not to be read into the claim, and applicant's arguments are unpersuasive since there is no explicit recitation in the claim describing the microfluidic proteome analysis system. If Applicant wishes have the described features of the proteome analysis system considered in determining patentability, they should be included in the claim.

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Applicant further argues that “a mere two dimensional protein separation apparatus” does not read on the microfluidic system for proteome analysis (Amendment page 16, lines 20-23) and further describes the system of Lee et al in distinguishing it from the proteome analysis system described in Applicant’s specification. (Amendment page 17, lines 4-24) In the absence of any further recitation of structure, the examiner respectfully submits that a system containing a microfluidic channel that is suitable for analysis of proteins - especially one suitable for resolving a large number of proteins, such as Lee et al - can be considered a proteome analysis system. Whether a proteome is analyzed is a matter of choice of sample composition, number of samples, and number of experiments within the skill of one having ordinary skill in the art. Any microfluidic capillary electrophoresis system suitable for analyzing protein mixtures can potentially be used in proteome analysis, and any of these would read on this limitation as currently claimed.

Applicant further argues that there would be no motivation to combine Xue et al with Lee et al, stating that neither reference suggests the need for further separation or combination with other devices. (Amendment page 17, lines 24-29) As stated above, because Xue et al and Lee et al are directed towards quite similar problems (i.e. separation of proteins by electrophoresis within capillary channels formed on a substrate), the examiner considers that it would have been within the abilities of a skilled artisan to incorporate such known related prior art channel geometries, connectivity, and separation strategies as taught by Lee et al into the system of Xue et

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al, given a protein sample of sufficient complexity that it would require multiple stages of separation.

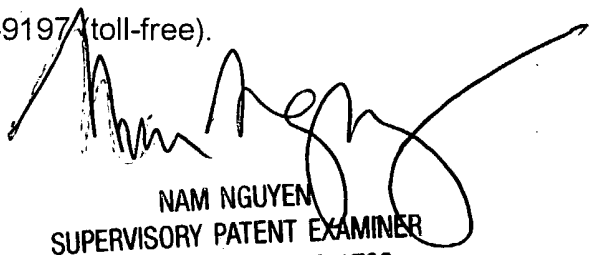
Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 toll-free).

JTB
January 4, 2005



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